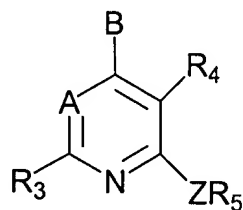


**Complete listing of claims:**

1-3. (Withdrawn)

4. (Currently amended) A pharmaceutical composition comprising a corticotropin releasing factor antagonist and a growth hormone secretagogue or growth hormone, wherein said corticotropin releasing factor antagonist is a compound of formula



wherein

A is CR<sub>7</sub> or N;

B is NR<sub>1</sub>R<sub>2</sub>, CR<sub>1</sub>R<sub>2</sub>R<sub>11</sub>, C(=CR<sub>2</sub>R<sub>12</sub>)R<sub>1</sub>, NHCHR<sub>1</sub>R<sub>2</sub>, OCHR<sub>1</sub>R<sub>2</sub>, SCHR<sub>1</sub>R<sub>2</sub>, CHR<sub>2</sub>OR<sub>12</sub>, CHR<sub>2</sub>SR<sub>12</sub>, C(S)R<sub>2</sub> or C(O)R<sub>2</sub>;

Z is NH, O, S, N (C<sub>1</sub>-C<sub>2</sub> alkyl), or CR<sub>13</sub>R<sub>14</sub>, wherein R<sub>13</sub> and R<sub>14</sub> are each independently hydrogen, trifluoromethyl, or C<sub>1</sub>-C<sub>4</sub> alkyl, or one of R<sub>13</sub> and R<sub>14</sub> may be cyano, chloro, bromo, iodo, fluoro, hydroxy, O(C<sub>1</sub>-C<sub>2</sub> alkyl), amino, NH(C<sub>1</sub>-C<sub>2</sub> alkyl), or CR<sub>13</sub>R<sub>14</sub> may be C=O or cyclopropyl;

R<sup>1</sup> is C<sub>1</sub>-C<sub>6</sub> alkyl which may be substituted by one or two substituents R<sub>8</sub> independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, C<sub>1</sub>-C<sub>4</sub> alkoxy, O-CO-(C<sub>1</sub>-C<sub>4</sub> alkyl), O-CO-NH(C<sub>1</sub>-C<sub>4</sub> alkyl), O-CO-N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), NH(C<sub>1</sub>-C<sub>4</sub> alkyl), N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), S(C<sub>1</sub>-C<sub>4</sub> alkyl), N(C<sub>1</sub>-C<sub>4</sub>alkyl)CO(C<sub>1</sub>-C<sub>4</sub> alkyl), NHCO(C<sub>1</sub>-C<sub>4</sub> alkyl), COO(C<sub>1</sub>-C<sub>4</sub> alkyl), CONH(C<sub>1</sub>-C<sub>4</sub> alkyl), CON(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), S(C<sub>1</sub>-C<sub>4</sub> alkyl), CN, NO<sub>2</sub>, SO(C<sub>1</sub>-C<sub>4</sub> alkyl), SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), and said C<sub>1</sub>-C<sub>4</sub> alkyl or C<sub>1</sub>-C<sub>4</sub> alkyl may contain one double or triple bond;

R<sub>2</sub> is C<sub>1</sub>-C<sub>12</sub> alkyl, aryl or (C<sub>1</sub>-C<sub>4</sub> alkylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or (C<sub>1</sub>-C<sub>6</sub> alkylene)cycloalkyl, wherein said cycloalkyl may contain one or two of O, S or N-R<sub>9</sub> wherein R<sub>9</sub> is hydrogen, or C<sub>1</sub>-C<sub>4</sub> alkyl,

wherein the above defined  $R_2$  may be substituted independently by from one to three of chloro, fluoro, or  $C_1$ - $C_4$  alkyl, or one of bromo, iodo,  $C_1$ - $C_6$  alkoxy,  $O$ - $CO$ -( $C_1$ - $C_6$  alkyl),  $O$ - $CO$ - $N$ ( $C_1$ - $C_4$  alkyl)( $C_1$ - $C_2$  alkyl),  $S$ ( $C_1$ - $C_6$  alkyl),  $CN$ ,  $NO_2$ ,  $SO$ ( $C_1$ - $C_4$  alkyl), or  $SO_2$ ( $C_1$ - $C_4$  alkyl), and wherein said  $C_1$ - $C_{12}$  alkyl or  $C_1$ - $C_4$  alkylene may contain one double or triple bond; or

$NR_1R_2$  or  $CR_1R_2R_{11}$  may form a saturated 5- to 8-membered carbocyclic ring which may contain one or two double bonds or one or two of  $O$  or  $S$ ;

$R_3$  is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy,  $OCF_3$ , methylthio, methylsulfonyl,  $CH_2OH$  or  $CH_2OCH_3$ ;

$R_4$  is hydrogen,  $C_1$ - $C_4$  alkyl, fluoro, chloro, bromo, iodo,  $C_1$ - $C_4$  alkoxy, amino, nitro,  $NH$ ( $C_1$ - $C_4$  alkyl),  $N$ ( $C_1$ - $C_4$  alkyl)( $C_1$ - $C_2$  alkyl),  $SO_n$ ( $C_1$ - $C_4$  alkyl), wherein  $n$  is  $O$ , 1 or 2, cyano, hydroxy,  $CO$ ( $C_1$ - $C_4$  alkyl),  $CHO$ , or  $COO$ ( $C_1$ - $C_4$  alkyl), wherein said  $C_1$ - $C_4$  alkyl may contain one or two double or triple bonds and may be substituted by one or two of hydroxy, amino, carboxy,  $NHCOCH_3$ ,  $NH$ ( $C_1$ - $C_2$  alkyl),  $N$ ( $C_1$ - $C_2$  alkyl) $_2$ ,  $COO$ ( $C_1$ - $C_4$  alkyl),  $CO$ ( $C_1$ - $C_4$  alkyl),  $C_1$ - $C_3$  alkoxy,  $C_1$ - $C_3$  thioalkyl, fluoro, chloro, cyano or nitro;

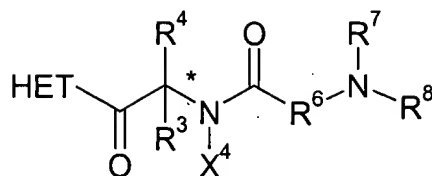
$R_5$  is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, furanyl, benzofuranyl, benzothiazolyl, or indolyl, wherein each one of the above groups  $R_5$  is substituted independently by from one to three of fluoro, chloro,  $C_1$ - $C_6$  alkyl, or  $C_1$ - $C_6$  alkoxy, or one of hydroxy, iodo, bromo, formyl, cyano, nitro, trifluoromethyl, amino,  $NH$ ( $C_1$ - $C_4$  alkyl),  $N$ ( $C_1$ - $C_6$ )( $C_1$ - $C_2$  alkyl),  $COOH$ ,  $COO$ ( $C_1$ - $C_4$  alkyl),  $CO$ ( $C_1$ - $C_4$  alkyl),  $SO_2NH$ ( $C_1$ - $C_4$  alkyl),  $SO_2N$ ( $C_1$ - $C_4$  alkyl)( $C_1$ - $C_2$  alkyl),  $SO_2NH_2$ ,  $NHSO_2$ ( $C_1$ - $C_4$  alkyl),  $S$ ( $C_1$ - $C_6$  alkyl), or  $SO_2$ ( $C_1$ - $C_6$  alkyl), wherein said  $C_1$ - $C_4$  alkyl and  $C_1$ - $C_6$  alkyl may be substituted by one or two of fluoro, hydroxy, amino, methylamino, dimethylamino or acetyl;

$R_7$  is hydrogen,  $C_1$ - $C_4$  alkyl, fluoro, chloro, bromo, iodo, cyano, hydroxy,  $O$ ( $C_1$ - $C_4$  alkyl),  $C(O)$ ( $C_1$ - $C_4$  alkyl), or  $C(O)O$ ( $C_1$ - $C_4$  alkyl), wherein the  $C_1$ - $C_4$  alkyl groups may be substituted with one hydroxy, chloro or bromo, or one to three fluoro;

$R^{11}$  is hydrogen, hydroxy, fluoro, or methoxy;

$R^{12}$  is hydrogen or  $C_1$ - $C_4$  alkyl; and

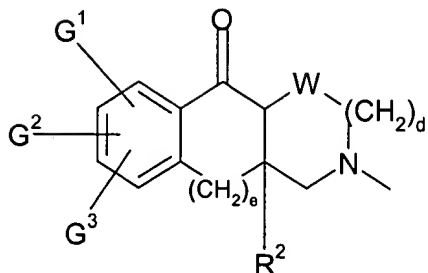
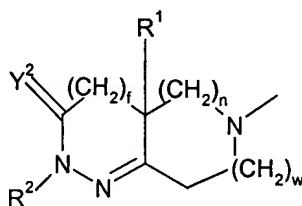
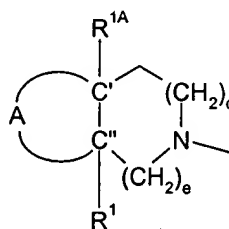
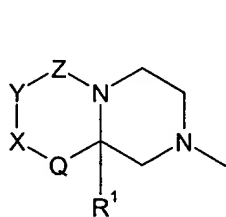
wherein said growth hormone secretagogue is a compound of formula IV:



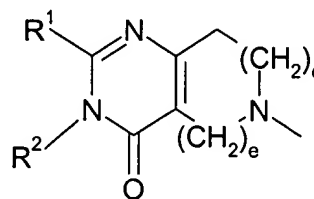
IV

or a stereoisomeric mixture thereof, a diastereomerically enriched, diastereomerically pure, enantiomerically enriched, or enantiomerically pure isomer thereof, or a prodrug of such compound, mixture, or isomer thereof, or a pharmaceutically acceptable salt of the compound, mixture, isomer, or prodrug, wherein in formula IV:

HET is a heterocyclic moiety selected from the group consisting of



and



d is 0, 1, or 2;

e is 1 or 2;

f is 0 or 1;

n and w are 0, 1, or 2, provided that n and w cannot both be 0 at the same time;

$Y^2$  is oxygen or sulfur;

A is a divalent radical, wherein the left hand side of the radical as shown below is connected to C" and the right hand side of the radical as shown below is connected C', selected from the group consisting of  $-NR^2-CO-NR^2-$ ,  $-NR^2-SO_2-NR^2-$ ,  $-O-CO-NR^2-$ ,  $-NR^2-CO_2-$ ,  $-CO-NR^2-CO-$ ,  $-CO-NR^2-C(R^9R^{10})-$ ,  $-C(R^9R^{10})-NR^2-CO-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-$ ,  $-SO_2-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-O-CO-$ ,  $-C(R^9R^{10})-O-C(R^9R^{10})-$ ,  $-NR^2-CO-C(R^9R^{10})-$ ,  $-O-CO-C(R^9R^{10})-$ ,  $-C(R^9R^{10})-CO-NR^2-$ ,  $-CO-NR^2-CO-$ ,  $-C(R^9R^{10})-CO_2-$ ,  $-CO-NR^2-C(R^9R^{10})-C(R^9R^{10})-CO_2-C(R^9R^{10})-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-$ ,  $-SO_2-NR^2-C(R^9R^{10})-C(R^9R^{10})-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-NR^2-CO-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-O-CO-$ ,  $-NR^2-CO-C(R^9R^{10})-C(R^9R^{10})-$ ,  $-NR^2-SO_2-C(R^9R^{10})-C(R^9R^{10})-$ ,  $-O-CO-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-$ ,  $-CO-NR^2-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-CO-$ ,  $-C(R^9R^{10})-NR^2-CO_2-C(R^9R^{10})-O-CO-NR^2-$ ,  $-C(R^9R^{10})-NR^2-CO-NR^2-$ ,  $-NR^2-CO_2-C(R^9R^{10})-$ ,  $-NR^2-CO-NR^2-C(R^9R^{10})-$ ,  $-NR^2-SO_2-NR^2-C(R^9R^{10})-$ ,  $-O-CO-NR^2-C(R^9R^{10})-$ ,  $-CO-N=C(R^{11})-NR^2-$ ,  $-CO-NR^2-C(R^{11})=N-$ ,  $-C(R^9R^{10})-NR^{12}-C(R^9R^{10})-$ ,  $-NR^{12}-C(R^9R^{10})-$ ,  $-NR^{12}-C(R^9R^{10})-C(R^9R^{10})-$ ,  $-CO_2-C(R^9R^{10})-C(R^9R^{10})-$ ,  $-NR^2-C(R^{11})=N-CO-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-N(R^{12})-$ ,  $-C(R^9R^{10})-NR^{12}-$ ,  $-N=C(R^{11})-NR^2-CO-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-NR^2-SO_2-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-SO_2-NR^2-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-CO_2-$ ,  $-C(R^9R^{10})-SO_2-C(R^9R^{10})-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-SO_2-$ ,  $-O-C(R^9R^{10})-C(R^9R^{10})-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-O-$ ,  $-C(R^9R^{10})-CO-C(R^9R^{10})-$ ,  $-CO-C(R^9R^{10})-C(R^9R^{10})-$ , and  $-C(R^9R^{10})-NR^2-SO_2-NR^2-$ ;

Q is a covalent bond or  $CH_2$ ;

W is CH or N;

X is  $CR^9R^{10}$ ,  $C=CH_2$ , or  $C=O$ ;

Y is  $CR^9R^{10}$ , O, or  $NR^2$ ;

Z is  $C=O$ ,  $C=S$ , or  $SO_2$ ;

$G^1$  is hydrogen, halo, hydroxy, nitro, amino, cyano, phenyl, carboxyl,  $-CONH_2$ ,  $-C_1-C_4$  alkyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups,  $-C_1-C_4$  alkoxy optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups,  $-C_1-C_4$  alkylthio, phenoxy,  $-CO_2-(C_1-C_4$  alkyl), N,N-di-( $C_1-C_4$  alkylamino),  $-C_2-C_6$  alkenyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups,  $-C_2-C_6$  alkynyl optionally independently substituted with one or more phenyl, one or more halogen, or one or

more hydroxy groups, -C<sub>3</sub>-C<sub>6</sub> cycloalkyl optionally independently substituted with one or more C<sub>1</sub>-C<sub>4</sub> alkyl groups, one or more halogen, or one or more hydroxy groups, -C<sub>1</sub>-C<sub>4</sub> alkylamino carbonyl, or di-C<sub>1</sub>-C<sub>4</sub> alkylamino) carbonyl;

G<sup>2</sup> and G<sup>3</sup> are each independently selected from the group consisting of hydrogen, halo, hydroxy, -C<sub>1</sub>-C<sub>4</sub> alkyl optionally independently substituted with one to three halo groups, and -C<sub>1</sub>-C<sub>4</sub> alkoxy optionally independently substituted with one to three halo groups;

R<sup>1</sup> is hydrogen, -CN, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>COX<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>CO(CH<sub>2</sub>)-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>SO<sub>2</sub>(CH<sub>2</sub>)-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>SO<sub>2</sub>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>CONX<sup>6</sup>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>CONX<sup>6</sup>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>CONX<sup>6</sup>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>CONX<sup>6</sup>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>CO<sub>2</sub>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>CO<sub>2</sub>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>OX<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>OOOX<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>OCO(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>OCONX<sup>6</sup>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>OCONX<sup>6</sup>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>COX<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>CO(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>CO<sub>2</sub>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>SO<sub>2</sub>NX<sup>6</sup>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>SO<sub>m</sub>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>SO<sub>m</sub>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -C<sub>1</sub>-C<sub>10</sub> alkyl, -(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>-(C<sub>3</sub>-C<sub>1</sub> cycloalkyl), -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(C<sub>1</sub>-C<sub>6</sub> alkyl), -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, or -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(CH<sub>2</sub>)<sub>t</sub>-(C<sub>3</sub>-C<sub>1</sub> cycloalkyl);

wherein the alkyl and cycloalkyl groups in the definition of R<sup>1</sup> are optionally substituted with C<sub>1</sub>-C<sub>4</sub> alkyl, hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy, carboxyl, -CONH<sub>2</sub>, -SO<sub>m</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl), -CO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl) ester, 1H-tetrazol-5-yl, or 1, 2, or 3 fluoro groups;

Y<sup>1</sup> is O, SO<sub>m</sub>, -CONX<sup>6</sup>-, -CH=CH-, -C=C-, -NX<sup>6</sup>CO-, -CONX<sup>6</sup>-, -CO<sub>2</sub>-, -OCONX<sup>6</sup>- or -OCO-;

q is 0, 1, 2, 3, or 4;

t is 0, 1, 2, or 3;

said (CH<sub>2</sub>)<sub>q</sub> group and (CHA group in the definition of R<sup>1</sup> are optionally independently substituted with hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy, carboxyl, -CONH<sub>2</sub>, -SO<sub>m</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl), -CO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl) ester, 1 H-tetrazol-5-yl, 1, 2, or 3 fluoro groups, or 1 or 2 C<sub>1</sub>-C<sub>4</sub> alkyl groups;

R<sup>1A</sup> is selected from the group consisting of hydrogen, F, Cl, Br, I, C<sub>1</sub>-C<sub>6</sub> alkyl, phenyl-(C<sub>1</sub>-C<sub>3</sub> alkyl), pyridyl-(C<sub>1</sub>-C<sub>3</sub> alkyl), thiazolyl-(C<sub>1</sub>-C<sub>3</sub> alkyl), and thienyl-(C<sub>1</sub>-C<sub>3</sub> alkyl), provided that R<sup>1A</sup> is not F, Cl, Br, or I when a heteroatom is vicinal to C<sup>''</sup>;

R<sup>2</sup> is hydrogen, C<sub>1</sub>-C<sub>8</sub> alkyl, -(C<sub>6</sub>-C<sub>3</sub> alkyl)-(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>1</sub>-C<sub>4</sub> alkyl)-A<sup>1</sup>, or A<sup>1</sup>, wherein the alkyl groups and the cycloalkyl groups in the definition of R<sup>2</sup> are optionally substituted with hydroxy, -CO<sub>2</sub> X<sup>6</sup>, -CONX<sup>6</sup>X<sup>6</sup>, -NX<sup>6</sup>X<sup>6</sup>, -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), -COA<sup>1</sup>, -COX<sup>6</sup>, CF<sub>3</sub>, CN, or 1, 2, or 3 independently selected halo groups;

$R^3$  is selected from the group consisting of  $A'$ ,  $C_1$ - $C_{10}$  alkyl,  $-(C_1$ - $C_6$  alkyl)- $A'$ ,  $-(C_1$ - $C_6$  alkyl)- $(C_3$ - $C_1$  cycloalkyl),  $-(C_1$ - $C_5$  alkyl)- $X'$ -( $C_1$ - $C_5$  alkyl),  $-(C_1$ - $C_5$  alkyl)- $X'$ -( $C_6$ - $C_5$  alkyl)- $A'$ , and  $-(C_1$ - $C_5$  alkyl)- $X'$ -( $C_1$ - $C_5$  alkyl)- $(C_3$ - $C_1$  cycloalkyl);

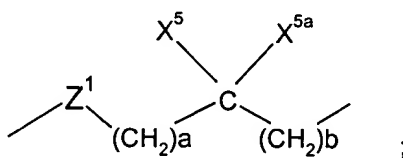
wherein the alkyl groups in the definition of  $R^3$  are optionally substituted with  $-SO_m(C_1$ - $C_6$  alkyl),  $-CO_2 X^3$ , 1, 2, 3, 4, or 5 independently selected halo groups, or 1, 2, or 3 independently selected  $-OX^3$  groups;

$X'$  is O,  $SO_m$ ,  $-NX^2CO-$ ,  $-CONX^2-$ ,  $-OCO-$ ,  $-CO_2-$ ,  $-CX^2=CX^2-$ ,  $-NX^2CO_2-$ ,  $-OCONX^2-$ , or  $-C\equiv C-$ ;

$R^4$  is hydrogen,  $C_1$ - $C_6$  alkyl, or  $C_3$ - $C_7$  cycloalkyl, or  $R^4$  taken together with  $R^3$  and the carbon atom to which they are attached form  $C_5$ - $C_1$  cycloalkyl,  $C_5$ - $C_1$  cycloalkenyl, a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, or a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, fused to a partially saturated, fully unsaturated, or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

$X^4$  is hydrogen or  $C_1$ - $C_6$  alkyl, or  $X^4$  is taken together with  $R^4$  and the nitrogen atom to which  $X^4$  is attached and the carbon atom to which  $R^4$  is attached and form a five to seven membered ring;

$R^6$  is a bond or is



wherein  $a$  and  $b$  are each independently O, 1, 2, or 3;

$X^5$  and  $X^{5a}$  are each independently selected from the group consisting of hydrogen,  $CF_3$ ,  $A'$ , and  $C_1$ - $C_6$  alkyl optionally substituted with  $A'$ ,  $OX^2$ ,  $-SO$ ,  $-(C_1$ - $C_6$  alkyl),  $-CO_2 X^2$ ,  $C_3$ - $C_7$  cycloalkyl,  $-NX^2X^2$ , or  $-CONX^2X^2$ ;

or the carbon bearing  $X^5$  or  $X^{5a}$  forms one or two alkylene bridges with the nitrogen atom bearing  $R^7$  and  $R^8$  wherein each alkylene bridge contains 1 to 5 carbon atoms, provided that when one alkylene bridge is formed then only one of  $X^5$  or  $X^{5a}$  is on the carbon atom and only one of  $R^7$  or  $R^8$  is on the nitrogen atom, and further provided that when two alkylene bridges are formed then  $X^5$  and  $X^{5a}$  cannot be on the carbon atom and  $R^7$  and  $R^8$  cannot be on

the nitrogen atom;

or  $X^5$  taken together with  $X^{5a}$  and the carbon atom to which they are attached form a partially saturated or fully saturated 3- to 7-membered ring, or a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen;

or  $X^5$  taken together with  $X^{5a}$  and the carbon atom to which they are attached form a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, optionally having 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

$Z^1$  is a bond, O, or  $N-X^2$ , provided that when a and b are both O then  $Z^1$  is not  $N-X^2$  or O;

$R^7$  and  $R^8$  are each independently hydrogen or  $C_1$ - $C_6$  alkyl optionally independently substituted with  $A^1$ ,  $-CO_2$ -( $C_1$ - $C_6$  alkyl),  $-SO_m$ -( $C_1$ - $C_6$  alkyl), 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3  $-O-CO$ -( $C_1$ - $C_{10}$  alkyl) groups, or 1 to 3  $C_1$ - $C_6$  alkoxy groups; or  $R^7$  and  $R^8$  can be taken together to form  $-(CH_2)_n$ ,  $L-(CH_2)_n-$ , wherein L is  $CX^2X^2$ ,  $SO_n$ , or  $NX^2$ ;

$R^9$  and  $R^{10}$  are each independently selected from the group consisting of hydrogen, fluoro, hydroxy, and  $C_1$ - $C_5$  alkyl optionally independently substituted with 1-5 halo groups;

$R^{11}$  is selected from the group consisting of  $C_1$ - $C_5$  alkyl and phenyl optionally substituted with 1-3 substituents each independently selected from the group consisting of  $C_1$ - $C_5$  alkyl, halo, and  $C_1$ - $C_5$  alkoxy;

$R^{12}$  is selected from the group consisting of  $C_1$ - $C_5$  alkylsulfonyl,  $C_1$ - $C_5$  alkanoyl, and  $C_1$ - $C_5$  alkyl wherein the alkyl portion is optionally independently substituted by 1-5 halo groups;

$A^1$  for each occurrence is independently selected from the group consisting of  $C_5$ - $C_7$  cycloalkenyl, phenyl, a partially saturated, fully saturated, or fully unsaturated 4 to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, and a bicyclic ring system consisting of a partially saturated, fully unsaturated, or fully saturated 5- or 6 membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

A<sup>1</sup> for each occurrence is independently optionally substituted, on one or optionally both rings if A' is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, Cl, Br, I, OCF<sub>3</sub>, OCF<sub>2</sub>H, CF<sub>3</sub>, CH<sub>3</sub>, OCH<sub>3</sub>, -OX<sup>6</sup>, -CONX<sup>6</sup>X<sup>6</sup>, -CO<sub>2</sub>X<sup>6</sup>, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, nitro, cyano, benzyl, -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), 1 H-tetrazol-5-yl, phenyl, phenoxy, phenylalkyloxy, halophenyl, methylenedioxy, -NX<sup>6</sup>X<sup>6</sup>, -NX<sup>6</sup>COX<sup>6</sup>, -SO<sub>2</sub>NX<sup>6</sup>X<sup>1</sup>, -NX<sup>6</sup>SO<sub>2</sub>-phenyl, NX<sup>6</sup>SO<sub>2</sub>X<sup>6</sup>, -CONX<sup>11</sup>X<sup>12</sup>, -SO<sub>2</sub>NX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>SO<sub>2</sub>X<sup>12</sup>, -NX<sup>6</sup>CONX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>SO<sub>2</sub>NX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>COX<sup>12</sup>, imidazolyl, thiazolyl, and tetrazolyl, provided that if A<sup>1</sup> is optionally substituted with methylenedioxy then it can only be substituted with one methylenedioxy;

wherein X<sup>11</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl optionally independently substituted with phenyl, phenoxy, C<sub>1</sub>-C<sub>6</sub> alkoxy carbonyl, -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3 C<sub>1</sub>-C<sub>10</sub> alkanoyloxy groups, or 1 to 3 C<sub>1</sub>-C<sub>6</sub> alkoxy groups;

X<sup>12</sup> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, phenyl, thiazolyl, imidazolyl, furyl, or thienyl, provided that when X<sup>2</sup> is not hydrogen, the X<sup>2</sup> group is optionally substituted with one to three substituents independently selected from the group consisting of Cl, F, CH<sub>3</sub>, OCH<sub>3</sub>, OCF<sub>3</sub>, and CF<sub>3</sub>;

or X<sup>1</sup> and X<sup>2</sup> are taken together to form -(CH<sub>2</sub>)<sub>r</sub>-L<sup>1</sup>-(CH<sub>2</sub>)<sub>r</sub>, wherein L<sup>1</sup> is CX<sup>2</sup>X<sup>2</sup>, O, SO<sub>m</sub> or NX<sup>2</sup>;

r for each occurrence is independently 1, 2, or 3;

X<sup>2</sup> for each occurrence is independently hydrogen, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, or optionally substituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl, wherein the optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl and optionally substituted C<sub>3</sub>-C<sub>1</sub> cycloalkyl in the definition of X<sup>2</sup> are optionally independently substituted with -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), -CO<sub>2</sub>X<sup>3</sup>, 1 to 5 halo groups, or 1-3 OX<sup>3</sup> groups;

X<sup>3</sup> for each occurrence is independently hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;

X<sup>6</sup> for each occurrence is independently hydrogen, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, halogenated C<sub>2</sub>-C<sub>6</sub> alkyl, optionally substituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl, halogenated C<sub>3</sub>-C<sub>7</sub> cycloalkyl, wherein the optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl and optionally substituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl in the definition of X<sup>6</sup> are optionally independently mono- or di-substituted with C<sub>1</sub>-C<sub>4</sub> alkyl, hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy, carboxyl, CONH<sub>2</sub>, -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), carboxylate (C<sub>1</sub>-C<sub>4</sub> alkyl) ester, or 1 H-tetrazol-5-yl; or

when there are two X<sup>6</sup> groups on one atom and both X<sup>6</sup> are independently C<sub>1</sub>-C<sub>6</sub> alkyl, the two C<sub>1</sub>-C<sub>6</sub> alkyl groups may be optionally joined, and together with the atom to which the two X<sup>6</sup>



groups are attached, form a 4- to 9- membered ring optionally having oxygen, sulfur, or  $NX^7$  as a ring member, wherein  $X^7$  is hydrogen or  $C_1-C_6$  alkyl optionally substituted with hydroxy;

m for each occurrence is independently 0, 1, or 2; with the provisos that:

$X^6$  and  $X^2$  cannot be hydrogen when attached to CO or  $SO_2$  in the form  $COX^6$ ,  $COX^2$ ,  $SO_2X^6$  or  $SO_2X^2$ ; and

when  $R^6$  is a bond then L is  $NX^2$  and each r in the definition  $-(CH_2)_r$ , L- $(CH_2)_r$ , is independently 2 or 3..

5-12. (Withdrawn)

13. (Currently amended) A pharmaceutical composition according to claim 4 wherein said corticotropin releasing factor antagonist is a compound selected from the group consisting of:

4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine;

4-(1-ethylpropoxy)-2,5-dimethyl-6-(2,4,6-trimethylphenoxy)-pyrimidine;

N-butyl-N-ethyl-2,5-dimethyl-NN-(2,4,6-trimethylphenyl)-pyrimidine-4,6diamine;

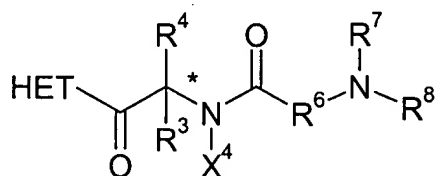
[4-(1-ethyl-propoxy)-3,6-dimethyl-pyridin-2-yl]-(2,4,6-trimethylphenyl)-amine;

[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-(1-ethyl-propyl)-amine;

[2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-(1-ethyl-propyl)-amine;

4-(1-ethyl-propylamino)-6-methyl-2-(2,4,6-trimethyl-phenoxy)-nicotinic acid methyl ester;

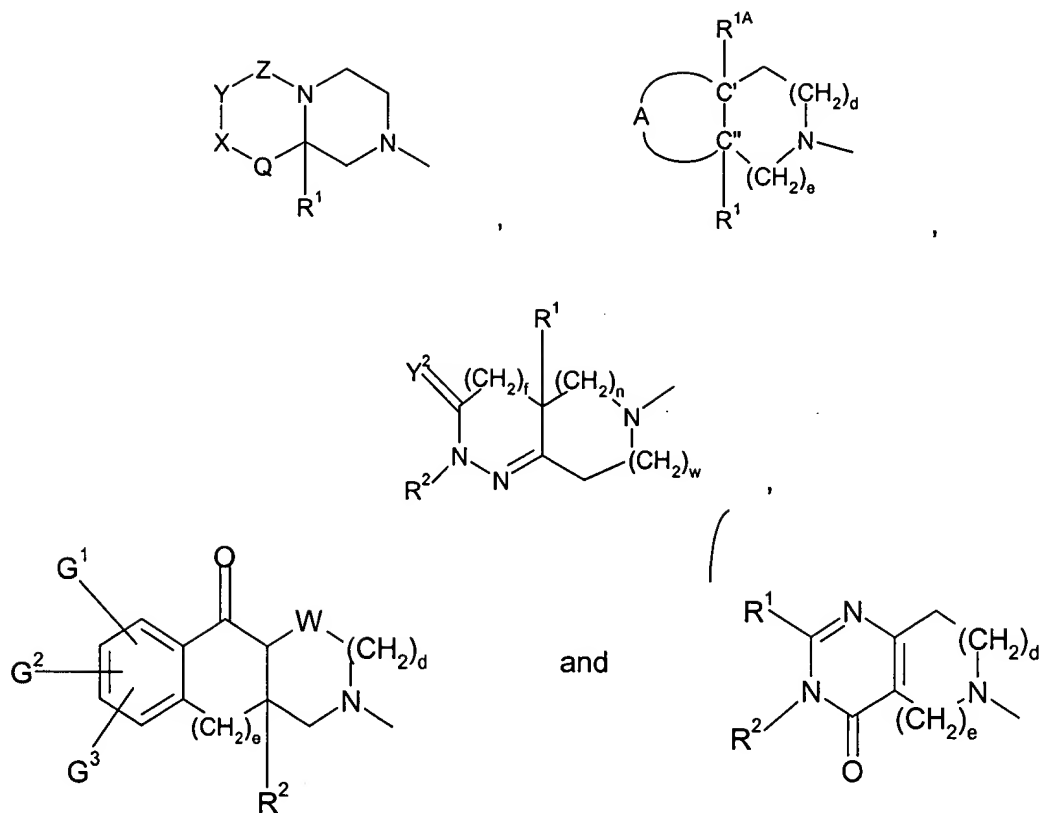
wherein said growth hormone secretagogue is a compound of formula IV:



IV

or a stereoisomeric mixture thereof, a diastereomerically enriched, diastereomerically pure, enantiomerically enriched, or enantiomerically pure isomer thereof, or a prodrug of such compound, mixture, or isomer thereof, or a pharmaceutically acceptable salt of the compound, mixture, isomer, or prodrug, wherein:

HET is a heterocyclic moiety selected from the group consisting of



d is  $\emptyset$ , 1, or 2;

e is 1 or 2;

f is  $\emptyset$  or 1;

n and w are  $\emptyset$ , 1, or 2, provided that n and w cannot both be  $\emptyset$  at the same time;

$Y^2$  is oxygen or sulfur;

A is a divalent radical, wherein the left hand side of the radical as shown below is connected to C'' and the right hand side of the radical as shown below is connected to C', selected from the group consisting of  $-NR^2-CO-NR^2-$ ,  $-NR^2-SO_2-NR^2-$ ,  $-O-CO-NR^2-$ ,  $-NR^2-CO_2-$ ,  $-CO-NR^2-CO-$ ,  $-CO-NR^2-C(R^9R^{10})-$ ,  $-C(R^9R^{10})-NR^2-CO-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-$ ,  $-SO_2-C(R^9R^{10})-C(R^9R^{10})-$ ,  $-C(R^9R^{10})-O-CO-$ ,  $-C(R^9R^{10})-O-C(R^9R^{10})-$ ,  $-NR^2-CO-C(R^9R^{10})-$ ,  $-O-CO-C(R^9R^{10})-$ ,  $-C(R^9R^{10})-CO-NR^2-$ ,  $-CO-NR^2-CO-$ ,  $-C(R^9R^{10})-CO_2-$ ,  $-CO-NR^2-C(R^9R^{10})-C(R^9R^{10})-I$ ,  $-CO_2-C(R^9R^{10})-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-C(R^9R^{10})-$ ,  $-SO_2-NR^2-C(R^9R^{10})-C(R^1R^{10})-$ ,  $-C(R^1R^{10})-C(R^9R^{10})-NR^2-CO-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-O-CO-$ ,  $-NR^2-CO-C(R^9R^{10})-$

C(R<sup>1</sup>R<sup>10</sup>)-NR<sup>2</sup>-SO<sub>2</sub>-C(R<sup>9</sup>R<sup>10</sup>)-C(R<sup>1</sup>R<sup>10</sup>)-O-CO-C(R<sup>9</sup>R<sup>10</sup>)-C(R<sup>9</sup>R<sup>10</sup>)-C(R<sup>9</sup>R<sup>10</sup>)-C(R<sup>9</sup>R<sup>10</sup>)-CO-NR<sup>2</sup>-, -C(R<sup>9</sup>R<sup>10</sup>)-C(R<sup>9</sup>R<sup>10</sup>)-CO-, -C(R<sup>9</sup>R<sup>10</sup>)-NR<sup>2</sup>-CO<sub>2</sub>-, -C(R<sup>9</sup>R<sup>10</sup>)-O-CO-NR<sup>2</sup>-, -C(R<sup>9</sup>R<sup>10</sup>)-NR<sup>2</sup>-CO-NR<sup>2</sup>-, -NR<sup>2</sup>-CO<sub>2</sub>-C(R<sup>9</sup>R<sup>10</sup>)-, -NR<sup>2</sup>-CO-NR<sup>2</sup>-C(R<sup>9</sup>R<sup>10</sup>)-, -NR<sup>2</sup>-SO<sub>2</sub>-NR<sup>2</sup>-C(R<sup>9</sup>R<sup>10</sup>)-, -O-CO-NR<sup>2</sup>-C(R<sup>9</sup>R<sup>10</sup>)-, -CO-N=C(R<sup>11</sup>)-NR<sup>2</sup>-, -CO-NR<sup>2</sup>-CR<sup>11</sup>=N-, CR<sup>9</sup>R<sup>10</sup>-NR<sup>12</sup>CR<sup>9</sup>R<sup>10</sup>-C(R<sup>9</sup>R<sup>10</sup>)-CO<sub>2</sub>-C(R<sup>9</sup>R<sup>10</sup>)-C(R<sup>9</sup>R<sup>10</sup>)-, -NR<sup>2</sup>-C(R<sup>11</sup>)=N-CO-C(R<sup>9</sup>R<sup>10</sup>)-C(R<sup>9</sup>R<sup>10</sup>)-N(R<sup>12</sup>)-C(R<sup>9</sup>R<sup>10</sup>)-NR<sup>12</sup>-, -N=C(R<sup>1</sup>)-NR<sup>2</sup>-CO-, -C(R<sup>9</sup>R<sup>10</sup>)-C(R<sup>9</sup>R<sup>10</sup>)-NR<sup>2</sup>-SO<sub>2</sub>-, -C(R<sup>9</sup>R<sup>10</sup>)-C(R<sup>9</sup>R<sup>10</sup>)-SO<sub>2</sub>-NR<sup>2</sup>-, -C(R<sup>9</sup>R<sup>10</sup>)-C(R<sup>9</sup>R<sup>10</sup>)-CO<sub>2</sub>-, -C(R<sup>9</sup>R<sup>10</sup>)-SO<sub>2</sub>-C(R<sup>9</sup>R<sup>10</sup>)-, -C(R<sup>9</sup>R<sup>10</sup>)-C(R<sup>9</sup>R<sup>10</sup>)-SO<sub>2</sub>-O-C(R<sup>9</sup>R<sup>10</sup>)-C(R<sup>9</sup>R<sup>10</sup>)-C(R<sup>9</sup>R<sup>10</sup>)-C(R<sup>9</sup>R<sup>10</sup>)-O-C(R<sup>9</sup>R<sup>10</sup>)-CO-C(R<sup>9</sup>R<sup>10</sup>)-, -CO-C(R<sup>9</sup>R<sup>10</sup>)-C(R<sup>9</sup>R<sup>10</sup>)-, and -C(R<sup>9</sup>R<sup>10</sup>)-NR<sup>2</sup>-SO<sub>2</sub>-NR<sup>2</sup>-;

Q is a covalent bond or CH<sub>2</sub>; W is CH or N;

X is CR<sup>9</sup>R<sup>10</sup>, C=CH<sub>2</sub>, or C=O; Y is CR<sup>9</sup>R<sup>10</sup>, O, or NR<sup>2</sup>;

Z is C=O, C=S, or SO<sub>2</sub>;

G<sup>1</sup> is hydrogen, halo, hydroxy, nitro, amino, cyano, phenyl, carboxyl, -CONH<sub>2</sub>, -C<sub>1</sub>-C<sub>4</sub> alkyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C<sub>1</sub>-C<sub>4</sub> alkoxy optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C<sub>1</sub>-C<sub>4</sub> alkylthio, phenoxy, -CO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl), N,N-di-(C<sub>1</sub>-C<sub>4</sub> alkylamino), -C<sub>2</sub>-C<sub>6</sub> alkenyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C<sub>2</sub>-C<sub>6</sub> alkynyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups, -C<sub>3</sub>-C<sub>6</sub> cycloalkyl optionally independently substituted with one or more C<sub>1</sub>-C<sub>4</sub> alkyl groups, one or more halogen, or one or more hydroxy groups, -C<sub>1</sub>-C<sub>4</sub> alkylamino carbonyl, or di-(C<sub>1</sub>-C<sub>4</sub> alkylamino) carbonyl;

G<sup>2</sup> and G<sup>3</sup> are each independently selected from the group consisting of hydrogen, halo, hydroxy, -C<sub>1</sub>-C<sub>4</sub> alkyl optionally independently substituted with one to three halo groups, and -C<sub>1</sub>-C<sub>4</sub> alkoxy optionally independently substituted with one to three halo groups;

R<sup>1</sup> is hydrogen, -CN, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>COX<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>CO(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>SO<sub>2</sub>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>SO<sub>2</sub>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>CONX<sup>6</sup>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>CONX<sup>6</sup>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>CONX<sup>6</sup>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>g</sub>CONX<sup>6</sup>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>CO<sub>2</sub>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>g</sub>CO<sub>2</sub>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>OX<sup>6</sup>, -(CH<sub>2</sub>)<sub>g</sub>OCOX<sup>6</sup>, -(CH<sub>2</sub>)<sub>g</sub>OOO(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>OOONX<sup>6</sup>(CHA-A<sup>1</sup>), -(CH<sub>2</sub>)<sub>q</sub>OOONX<sup>6</sup>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>COX<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>CO(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>CO<sub>2</sub>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>SO<sub>2</sub>NX<sup>6</sup>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>g</sub>SO<sub>m</sub>X<sup>6</sup>-(CH<sub>2</sub>)<sub>t</sub>SO<sub>m</sub>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -C<sub>1</sub>-C<sub>10</sub> alkyl, -(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>-(C<sub>3</sub>-C<sub>1</sub> cycloalkyl), -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(C<sub>1</sub>-C<sub>6</sub> alkyl), -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, or -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-

$(CH_2)_t$ -(C<sub>3</sub>-C<sub>1</sub> cycloalkyl);

wherein the alkyl and cycloalkyl groups in the definition of R' are optionally substituted with C<sub>1</sub>-C<sub>4</sub> alkyl, hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy, carboxyl, -CONH<sub>2</sub>, -SO<sub>m</sub> (C<sub>1</sub>-C<sub>6</sub> alkyl), -CO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl) ester, 1 H-tetrazol-5-yl, or 1, 2, or 3 fluoro groups;

Y' is O, SO<sub>m</sub>, -CONX<sup>6</sup>-, -CH=CH-, -C=C-, -NX<sup>6</sup>CO-, -CONX<sup>6</sup>-, -CO<sub>2</sub>-, -OCONX<sup>6</sup>- or -OCO-;

q is 0, 1, 2, 3, or 4; t is 0, 1, 2, or 3;

said (CH<sub>2</sub>)<sub>g</sub> group and (CH<sub>A</sub>) group in the definition of R' are optionally independently substituted with hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy, carboxyl, -CONH<sub>2</sub>, -SO<sub>m</sub> (C<sub>1</sub>-C<sub>6</sub> alkyl), -CO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl) ester, 1 H-tetrazol-5-yl, 1, 2, or 3 fluoro groups, or 1 or 2 C<sub>1</sub>-C<sub>4</sub> alkyl groups;

R<sup>1A</sup> is selected from the group consisting of hydrogen, F, Cl, Br, I, C<sub>1</sub>-C<sub>6</sub> alkyl, phenyl-(C<sub>1</sub>-C<sub>3</sub> alkyl), pyridyl-(C<sub>1</sub>-C<sub>3</sub> alkyl), thiazolyl-(C<sub>1</sub>-C<sub>3</sub> alkyl), and thienyl-(C<sub>1</sub>-C<sub>3</sub> alkyl), provided that R<sup>1A</sup> is not F, Cl, Br, or I when a heteroatom is vicinal to C'';

R<sup>2</sup> is hydrogen, C<sub>1</sub>-C<sub>8</sub> alkyl, -(C<sub>6</sub>-C<sub>3</sub> alkyl)-(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>1</sub>-C<sub>4</sub> alkyl)-A', or A', wherein the alkyl groups and the cycloalkyl groups in the definition of R<sup>2</sup> are optionally substituted with hydroxy, -CO<sub>2</sub> X<sup>6</sup>, -CONX<sup>6</sup>X<sup>6</sup>, -NX<sup>6</sup>X<sup>6</sup>, -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), -COA', -COX<sup>6</sup>, CF<sub>3</sub>, CN, or 1, 2, or 3 independently selected halo groups;

R<sup>3</sup> is selected from the group consisting of A', C<sub>1</sub>-C<sub>10</sub> alkyl, -(C<sub>1</sub>-C<sub>6</sub> alkyl)-A', -(C<sub>1</sub>-C<sub>6</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl), -(C<sub>1</sub>-C<sub>5</sub> alkyl)-X'-(C<sub>1</sub>-C<sub>5</sub> alkyl), -(C<sub>1</sub>-C<sub>5</sub> alkyl)-X'-(C<sub>6</sub>-C<sub>5</sub> alkyl)-A', and -(C<sub>1</sub>-C<sub>5</sub> alkyl)-X'-(C<sub>1</sub>-C<sub>5</sub> alkyl)-(C<sub>3</sub>-C<sub>1</sub> cycloalkyl);

wherein the alkyl groups in the definition of R<sup>3</sup> are optionally substituted with -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), -CO<sub>2</sub> X<sub>3</sub>, 1, 2, 3, 4, or 5 independently selected halo groups, or 1, 2, or 3 independently selected -OX<sup>3</sup> groups;

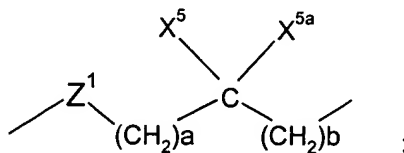
X' is O, SO, -NX<sup>2</sup>CO-, -CONX<sup>2</sup>-, -OCO-, -CO<sub>2</sub>-, -CX<sup>2</sup>=CX<sup>2</sup>-, -NX<sup>2</sup>CO<sub>2</sub>-, -OCONX<sup>2</sup>-, or -C-C-;

R<sup>4</sup> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, or R<sup>4</sup> taken together with R<sup>3</sup> and the carbon atom to which they are attached form C<sub>5</sub>-C<sub>1</sub> cycloalkyl, C<sub>5</sub>-C<sub>1</sub> cycloalkenyl, a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, or a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, fused to a partially saturated, fully unsaturated, or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen,

sulfur, and oxygen;

$X^4$  is hydrogen or  $C_1$ - $C_6$  alkyl, or  $X^4$  is taken together with  $R^4$  and the nitrogen atom to which  $X^4$  is attached and the carbon atom to which  $R^4$  is attached and form a five to seven membered ring;

$R^6$  is a bond or is



wherein a and b are each independently  $\in \{0, 1, 2, 3\}$ ;

$X^5$  and  $X^{5a}$  are each independently selected from the group consisting of hydrogen,  $CF_3$ ,  $A^1$ , and  $C_1$ - $C_6$  alkyl optionally substituted with  $A'$ ,  $OX^2$ ,  $-SO_2(C_1-C_6 \text{ alkyl})$ ,  $-CO_2 X^2$ ,  $C_3-C_1$  cycloalkyl,  $-NX^2X^2$ , or  $-CONX^2X^2$ ;

or the carbon bearing  $X^5$  or  $X^{5a}$  forms one or two alkylene bridges with the nitrogen atom bearing  $R^7$  and  $R^8$  wherein each alkylene bridge contains 1 to 5 carbon atoms, provided that when one alkylene bridge is formed then only one of  $X^5$  or  $X^{5a}$  is on the carbon atom and only one of  $R^7$  or  $R^8$  is on the nitrogen atom, and further provided that when two alkylene bridges are formed then  $X^5$  and  $X^{5a}$  cannot be on the carbon atom and  $R^7$  and  $R^8$  cannot be on the nitrogen atom;

or  $X^5$  taken together with  $X^{5a}$  and the carbon atom to which they are attached form a partially saturated or fully saturated 3- to 7-membered ring, or a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen;

or  $X^5$  taken together with  $X^{5a}$  and the carbon atom to which they are attached form a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, optionally having 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and

oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

$Z^1$  is a bond, O, or  $N-X^2$ , provided that when a and b are both 0 then  $Z^1$  is not  $N-X^2$  or O;

$R^7$  and  $R^8$  are each independently hydrogen or  $C_1$ - $C_6$  alkyl optionally independently substituted with  $A'$ ,  $-CO_2(C_1-C_6 \text{ alkyl})$ ,  $-SO_m(C_1-C_6 \text{ alkyl})$ ; 1 to 5 halo groups, 1 to 3

hydroxy groups, 1 to 3 -O-CO(C<sub>1</sub>-C<sub>10</sub> alkyl) groups, or 1 to 3 C<sub>1</sub>-C<sub>6</sub> alkoxy groups; or R' and R<sup>8</sup> can be taken together to form -(CH<sub>2</sub>)<sub>r</sub>, L-(CH<sub>2</sub>)<sub>r</sub>, wherein L is CX<sup>2</sup>X<sup>2</sup>, SO<sub>m</sub>, or NX<sup>2</sup>; R<sup>9</sup> and R<sup>9</sup> are each independently selected from the group consisting of hydrogen, fluoro, hydroxy, and C<sub>1</sub>-C<sub>5</sub> alkyl optionally independently substituted with 1-5 halo groups; R<sup>11</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>5</sub> alkyl and phenyl optionally substituted with 1-3 substituents each independently selected from the group consisting of C<sub>1</sub>-C<sub>5</sub> alkyl, halo, and C<sub>1</sub>-C<sub>5</sub> alkoxy; R<sup>12</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>5</sub> alkylsulfonyl, C<sub>1</sub>-C<sub>5</sub> alkanoyl, and C<sub>1</sub>-C<sub>5</sub> alkyl wherein the alkyl portion is optionally independently substituted by 1-5 halo groups; A' for each occurrence is independently selected from the group consisting of C<sub>5</sub>-C<sub>7</sub> cycloalkenyl, phenyl, a partially saturated, fully saturated, or fully unsaturated 4- to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, and a bicyclic ring system consisting of a partially saturated, fully unsaturated, or fully saturated 5- or 6- membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and 3Θ oxygen; A<sup>1</sup> for each occurrence is independently optionally substituted, on one or optionally both rings if A' is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, Cl, Br, I, OCF<sub>3</sub>, OCF<sub>2</sub>H, CF<sub>3</sub>, CH<sub>3</sub>, OCH<sub>3</sub>, -OX<sup>6</sup>, -CONX<sup>6</sup>X<sup>6</sup>, -CO<sub>2</sub>X<sup>6</sup>, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, nitro, cyano, benzyl, -SO<sub>l</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), 1 H-tetrazol-5-yl, phenyl, phenoxy, phenylalkyloxy, halophenyl, methylenedioxy, -NX<sup>6</sup>X<sup>6</sup>, -NX<sup>6</sup>COX<sup>6</sup>, -SO<sub>2</sub>NX<sup>6</sup>X<sup>6</sup>, -NX<sup>6</sup>SO<sub>2</sub>-phenyl, NX<sup>6</sup>SOX, -CONX<sup>11</sup>X<sup>12</sup>, -SO<sub>2</sub>NX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>SO<sub>2</sub>X<sup>12</sup>, -NX<sup>6</sup>CONX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>SO<sub>2</sub>NX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>COX<sup>12</sup>, imidazolyl, thiazolyl, and tetrazolyl, provided that if A' is optionally substituted with methylenedioxy then it can only be substituted with one methylenedioxy; wherein X<sup>11</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl optionally independently substituted with phenyl, phenoxy, C<sub>1</sub>-C<sub>5</sub> alkoxycarbonyl, -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3 C<sub>1</sub>-C<sub>10</sub> alkanoyloxy groups, or 1 to 3 C<sub>1</sub>-C<sub>6</sub> alkoxy groups; X<sup>12</sup> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, phenyl, thiazolyl, imidazolyl, furyl, or thienyl, provided that when X<sup>12</sup> is not hydrogen, the X<sup>12</sup> group is optionally substituted with one to three

substituents independently selected from the group consisting of Cl, F, CH<sub>3</sub>, OCH<sub>3</sub>, OCF<sub>3</sub>, and CF<sub>3</sub>;

or X<sup>11</sup> and X<sup>12</sup> are taken together to form -(CH<sub>2</sub>)<sub>r</sub>L<sup>1</sup>(CH<sub>2</sub>)<sub>r</sub>, wherein L<sup>1</sup> is CX<sup>2</sup>X<sup>2</sup>, O, SO, or NX<sup>2</sup>;

r for each occurrence is independently 1, 2, or 3;

X<sup>2</sup> for each occurrence is independently hydrogen, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, or optionally substituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl, wherein the optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl and optionally substituted C<sub>3</sub>-C<sub>1</sub> cycloalkyl in the definition of X<sup>2</sup> are optionally independently substituted with -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), -CO<sub>2</sub> X<sup>3</sup>, 1 to 5 halo groups, or 1-3 OX<sup>3</sup> groups;

X<sup>3</sup> for each occurrence is independently hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;

X<sup>6</sup> for each occurrence is independently hydrogen, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, halogenated C<sub>2</sub>-C<sub>6</sub> alkyl, optionally substituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl, halogenated C<sub>3</sub>-C<sub>7</sub> cycloalkyl, wherein the optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl and optionally substituted C<sub>3</sub>-C<sub>1</sub> cycloalkyl in the definition of X<sup>6</sup> are optionally independently mono or di-substituted with C<sub>1</sub>-C<sub>4</sub> alkyl, hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy, carboxyl, CONH<sub>2</sub>, -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), carboxylate (C<sub>1</sub>-C<sub>4</sub> alkyl) ester, or 1 H-tetrazol-5-yl; or

when there are two X<sup>6</sup> groups on one atom and both X<sup>6</sup> are independently C<sub>1</sub>-C<sub>6</sub> alkyl, the two C<sub>1</sub>-C<sub>6</sub> alkyl groups may be optionally joined, and together with the atom to which the two X<sup>6</sup> groups are attached, form a 4- to 9- membered ring optionally having oxygen, sulfur, or NX<sup>7</sup> as a ring member, wherein X<sup>7</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with hydroxy;

m for each occurrence is independently O, 1, or 2; with the provisos that:

X<sup>6</sup> and X<sup>12</sup> cannot be hydrogen when attached to CO or SO<sub>2</sub> in the form COX<sup>6</sup>, COX<sup>12</sup>, SO<sub>2</sub>X<sup>6</sup> or SO<sub>2</sub>X<sup>12</sup>; and

when R<sup>6</sup> is a bond then L is NX<sup>2</sup> and each r in the definition -(CH<sub>2</sub>)<sub>r</sub>L-(CH<sub>2</sub>)<sub>r</sub> is independently 2 or 3.

14. (Previously amended) A pharmaceutical composition according to claim 13 wherein said corticotropin releasing factor antagonist is a compound selected from the group consisting of:

4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine;

4-(1-ethyl propoxy)-2,5-dimethyl-6-(2,4,6-trimethyl phenoxy)-pyrimidine;

[4-(1-ethyl-propoxy)-3,6-dimethyl-pyridin-2-yl]-(2,4,6-trimethylphenyl)-amine;

[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-(1-ethyl-propyl)-amine;

15. (Cancelled)

16. (Previously amended) A pharmaceutical composition according to claim 4 wherein said growth hormone secretagogue is

2-amino-N-(2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydropyrazolo-[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl)isobutyramide;

2-amino-N-(1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a(R)-pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide;

2-amino-N-{1(R)-benzyloxymethyl-2-[1,3-dioxo-8a(S)-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxoethyl}-2-methyl-propionamide;

N-(1(R)-((1,2-dihydro-1-methanesulfonyl-spiro(3H-indole-3,4'-piperidin)-1'-yl)carbonyl)-2-(phenylmethoxy)ethyl)-2-amino-2-methylpropanamide; or

a prodrug of any of these compounds or a pharmaceutically acceptable salt of any of said compounds or said prodrugs.

17. (Cancelled)

18. (Previously amended) A pharmaceutical composition according to claim 13 wherein said growth hormone secretagogue is

2-amino-N-(2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl)-isobutyramide;

2-amino-N-(1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a-(R)-pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide;

2-amino-N-{1(R)-benzyloxymethyl-2-[1,3-dioxo-8a(S)-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxo-ethyl}-2-methyl-propionamide;

N-(1(R)-((1,2-dihydro-1-methanesulfonyl-spiro(3H-indole-3,4'-piperidin)-1'-yl)carbonyl)-2-(phenylmethyl oxy)ethyl)-2-amino-2-methyl-propanamide; or

a prodrug of any of these compounds, or a pharmaceutically acceptable salt of any of these compounds or prodrugs.

19. (Original) A pharmaceutical composition according to claim 18 wherein said corticotropin releasing factor antagonist is 4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-



trimethylphenoxy)-pyridine and said growth hormone secretagogue is 2-amino-N-[2-(3a(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide.

20. (Original) A pharmaceutical composition according to claim 18 wherein said corticotropin releasing factor antagonist is 4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine and said growth hormone secretagogue is 2-amino-N-(1(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a(R)-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide.

21. (Original) A pharmaceutical composition according to claim 18 wherein said corticotropin releasing factor antagonist is (3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl)-(1-ethyl-propyl)-amine and said growth hormone secretagogue is 2-amino-N-[2-(3a(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide.

22. (Original) A pharmaceutical composition according to claim 18 wherein said corticotropin releasing factor antagonist is (3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl)-(1-ethyl-propyl)-amine and said growth hormone secretagogue is 2-amino-N-(1(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a(R)-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide.

23-29. (Withdrawn)

30. (Previously amended) A kit comprising:

- a. an amount of a corticotropin releasing factor antagonist as defined in claim 13, in a first unit dosage form;
- b. an amount of a growth hormone secretagogue or growth hormone as defined in Claim 4, in a second unit dosage form; and
- c. a container.

31. (Previously amended) A kit comprising:

- a. an amount of a corticotropin releasing factor antagonist as defined in claim 14, in a first unit dosage form;
- b. an amount of a growth hormone secretagogue or growth hormone as defined in Claim 4, in a second unit dosage form; and
- c. a container.

32. (Withdrawn)

33. (Previously amended) A kit according to claim 30 wherein said corticotropin releasing factor antagonist is 4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine or [3,6-dimethyl-2-(2,4,6-dimethyl-phenoxy)-pyridin-4-yl]-(1-ethyl-propyl)-amine, and said growth hormone secretagogue is 2-amino-N-[2-(3a(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1 (R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide or 2-amino-N-(1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a-(R)-pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide.

34-35. (Withdrawn)